## **Supplementary information**

# The emerging role of photoacoustic imaging in clinical oncology

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#### **Common PACT detection configurations**

In photoacoustic computed tomography (PACT), the entire region of interest is typically excited by an expanded laser beam for wide-field illumination. To detect photoacoustic waves at multiple view angles, PACT usually uses an ultrasonic transducer array, allowing fast cross-sectional or volumetric imaging speeds. Ultrasonic transducer arrays with various populating patterns, such as line, plane, ring, and hemisphere<sup>1</sup>, have been demonstrated in clinical applications.

- (1) Linear and planar detection: Typically, a multimode optical fibre bundle is flanked by the linear array to provide illumination<sup>2</sup>. Each laser pulse yields a cross-sectional image, the thickness of which is determined by the array's focus. Despite the simplicity and versatility of this approach, the limited field of view (FOV) makes this approach less suitable for high-speed screening applications. Planar detection apertures can provide a larger FOV at the expense of higher system cost, however, the narrow view angles<sup>3</sup> of both linear and planar detection apertures limit such systems to features with specific orientations only and thus reduces both the image clarity and accuracy.
- (2) Cylindrical detection: Unlike partial-view detection in linear-array PACT, all photoacoustic waves propagating within the imaging plane can be detected by a circular array, regardless of their direction of propagation. Accordingly, full-view detection provides images with higher quality while reliably capturing relevant physiological features<sup>4,5</sup>. Of note, cylindrical detection geometry usually provides coarser elevational resolution than that of in-plane resolution, the latter of which is typically in the range of 0.1–0.5 mm.
- (3) Hemispherical detection: Unlike ring-array-based cylindrical detection, PACT using hemispherical detection configurations enables the detection of photoacoustic signals propagating along the elevational direction<sup>6</sup>, although this setup is typically unsuitable for real-time (faster than a heartbeat) imaging with a large FOV. Nonetheless, the improved elevational resolution provided by this setup is helpful for revealing finer imaging features.

#### **Engineering guidelines for PACT**

From the engineering perspective, a well-designed PACT system should have: (1) a sufficient noise-equivalent sensitivity<sup>7</sup> and contrast-to-noise ratio in deep tissue; (2) a large FOV with minimal imaging artefacts; (3) a high level of spatial resolution, thus enabling the detection of detailed structures; and

(4) a high imaging speed in order to minimize the incidence of motion artefacts and enable accurate dynamic and/or functional measurements. While the intensity of light illumination mainly determines criterion (1), and partially governs criteria (2) and (4), the acoustic detection affects all of these criteria.

To satisfy the criteria above, PACT engineers should consider: (1) optimized illumination schemes to provide relatively homogenous illumination within the FOV (imaging plane or volume); (2) optimized detection schemes that can provide both a large view angle<sup>3</sup> and spatially dense sampling<sup>8</sup>; (3) low-noise signal amplification and digitization circuits with proper grounding and shielding; (4) a steady scanning mechanism and safe operation procedure for reliable imaging performance; and (5) stable image reconstruction and processing algorithms that can maintain information from raw signals without enhancement of the artefact.

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